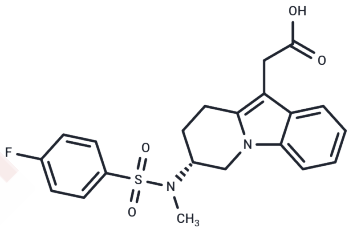
Data Sheet (Cat.No.TQ0051)

TargetMol

MK-7246

Chemical Properties



CAS No. : 1218918-62-7

Formula: C21H21FN2O4S

Molecular Weight: 416.47

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	MK-7246 is a potent and specific CRTH2 antagonist (Ki: 2.5 nM).
Targets(IC50)	GPCR,Prostaglandin Receptor
In vitro	MK-7246 competes for [3H]PGD2 specific binding to cell membranes expressing recombinant human CRTH2 with high-affinity (Ki, 2.5 nM). MK-7246 displays relatively high selectivity for CRTH2 with an affinity 149-fold lower for the DP receptor (Ki, 373±96 nM) and ≥1500-fold lower for the other prostanoid receptors (Ki, 7668±2169 nM for EP2, 3804±1290 nM for TP). MK-7246 is also tested in a panel of 157 enzyme and receptor assays at concentrations up to 100 μM and small but significant activity is detected only on phosphodiesterase 1 (PDE1, IC50=33.2 μM) and MAPK3 (ERK1, IC50=49.4 μM) [1].
In vivo	The study investigates whether inhibiting the clinically relevant CRTH2 mechanism of allergic lung inflammation suppresses inflammatory responses in A. alternata-challenged Brown Norway rats (n=8 per group). CRTH2 inhibitor MK-7246 is administered orally 1 hour before and 23 hours after intratracheal instillation of A. alternata. MK-7246 shows a dose-dependent decrease in eosinophil counts, with maximal inhibition of 74±5% at 100 mg/kg (P<0.05), and reduces IL-5 (80±12%) and IL-13 (76±14%) cytokine levels (P<0.05) [2].
Kinase Assay	The binding kinetics of [3H]MK-7246 (specific activity, 41 Ci/mmol) at human CRTH2 is characterized using recombinant HEK293E cell membranes. The radioligand binding experimental condition for CRTH2 as follows: the incubation mixture contains 10 mM MgCl2 instead of MnCl2, 10 nM [3H]MK-7246, and 1.25 μg of membrane protein. Total binding represents 10% of the radioligand adds to the incubation media, and specific binding at equilibrium corresponded to 85 to 95% of the total binding. The membranes are first incubated with [3H]MK-7246 for 120 min in the absence (total binding) or presence (nonspecific binding) of 10 μM MK-7246. To one series of total binding incubation tubes, 10 μM MK-7246 or 100 μM PGD2 is added to initiate dissociation of the radioligand from the receptor, and the reaction is left to proceed for up to 300 min. The samples are then harvested and processed as detailed above. The association and dissociation kinetic data analysis is done by nonlinear regression curve-fitting using Prism software to determine the observed on rate (Kobs) and dissociation rate (koff) constants, and t1/2 of on and off rates [1].

Animal Research	Intratracheal Budesonide is dosed 1 h prior to and 23 h post the A. alternate intratracheal dose while oral Budesonide (3 mg/kg) is administered 2 h before and 22 h post the A. alternata extract instillation. An intratracheally dosed Budesonide is prepared. MK-7246 (3, 10, 30 and 100 mg/kg) is administered orally 1 h before and 23 h post an A. alternata extract instillation in order to examine the effect of the CRTH2 antagonist on A. alternata elicited pulmonary inflammatory responses. Budesonide dosed orally is used as a positive control in both experiments. The animals are lightly anesthetized with 3% Isoflurane (supplemented with 100% oxygen), either 2 h following oral dosing or 1 h following intratracheal dosing. The animals are also secured on a rodent work stand to facilitate the localization of the larynx and tracheal openings. The micro sprayer needle is inserted into the trachea and 0.1 mL of 10,000 μg/mL (total of 1000 μg) A. alternata extract is administered using a micro sprayer. The animals are observed until they recover from anesthesia and then return to their cages and allow food and water ad libitum [2].

Solubility Information

Solubility	DMSO: 245 mg/mL (588.28 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 4 mg/mL (9.6 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4011 mL	12.0057 mL	24.0113 mL
5 mM	0.4802 mL	2.4011 mL	4.8023 mL
10 mM	0.2401 mL	1.2006 mL	2.4011 mL
50 mM	0.048 mL	0.2401 mL	0.4802 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Gervais FG, et al. Pharmacological characterization of MK-7246, a potent and selective CRTH2 (chemoattractant receptor-homologous molecule expressed on T-helper type 2 cells) antagonist. Mol Pharmacol. 2011 Jan;79(1):69-76.

Gil MA, et al. Anti-inflammatory actions of Chemoattractant Receptor-homologous molecule expressed on Th2 by the antagonist MK-7246 in a novel rat model of Alternaria alternata elicited pulmonary inflammation. Eur J Pharmacol. 2014 Nov 15;743:106-16.

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